

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
14 October 2004 (14.10.2004)

PCT

(10) International Publication Number
WO 2004/087870 A2

550 220

(51) International Patent Classification⁷: C12N
(21) International Application Number: PCT/US2004/009051
(22) International Filing Date: 24 March 2004 (24.03.2004)
(25) Filing Language: English
(26) Publication Language: English
(30) Priority Data:
60/457,383 25 March 2003 (25.03.2003) US

(74) Agent: HAILE, Lisa, A.; Gary Cary Ware & Friedenrich
LLP, Suite 1100, 4365 Executive Drive, San Diego, CA
92121-2133 (US).

(81) Designated States (*unless otherwise indicated, for every
kind of national protection available*): AE, AG, AL, AM,
AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,
MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG,
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW.

(63) Related by continuation (CON) or continuation-in-part
(CIP) to earlier application:
US 60/457,383 (CON)
Filed on 25 March 2003 (25.03.2003)

(84) Designated States (*unless otherwise indicated, for every
kind of regional protection available*): ARIPO (BW, GH,
GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),
Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), Euro-
pean (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR,
GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK,
TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,
ML, MR, NE, SN, TD, TG).

(71) Applicant (*for all designated States except US*): THE
JOHNS HOPKINS UNIVERSITY [US/US]; Licensing
and Technology Development, 3400 N. Charles Street,
Baltimore, MD 21218 (US).

Published:

— *without international search report and to be republished
upon receipt of that report*

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): BEACHY, Philip,
A. [US/US]; 7818 Chelsea Street, Towson, MD 21204
(US). COOPER, Michael, K. [US/US]; 2008 20th Avenue
South, Nashville, TN 37212 (US).

*For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.*

(54) Title: NEURONAL CELL LINEAGES AND METHODS OF PRODUCTION THEREOF

(57) Abstract: Methods are provided in which a sterol-depleting agent such as β -cyclodextrin (β CD), is used to modulate signaling by a differentiation signaling protein such as Hedgehog protein or a BMP *in vitro*. As illustrated herein, the use of β CD in conjunction with Sonic Hedgehog N-terminal peptide (ShhN) causes substantially all of the cells in neural plate explants to differentiate as neurons, such as motor neurons. Also provided are cell therapy methods and screening methods that rely on the modulation of signaling of a differentiation signaling protein such as Hedgehog, by a sterol-depleting agent such as β CD.



WO 2004/087870 A2